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Paper

Prevalence of patent foramen ovale in a consecutive cohort of 261 patients undergoing routine "coronary" 64-multi-detector cardiac computed tomography.

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ABSTRACT

Background: A patent foramen ovale (PFO) is strongly associated with cryptogenic stroke (CS), neurological and other phenomena. The reported prevalence of PFO varies according to the imaging technique used and population studied.

Purpose: To measure prospectively, the prevalence of PFO in a cohort of consecutive patients attending for routine "coronary" CT angiography using standard, everyday coronary protocols including low-dose prospective ECG gated studies.

Methods: Standard coronary imaging protocols were used. PFOs were graded according to the classification of Williamson *et al*.[1]

Results: 261 patients were studied. A PFO was identified in 22.6% (11.5% grade 1 (closed flap), 6.5% grade 2 (open flap) and 4.6% grade 3 (open flap with jet)). A further 6.1% had an atrial septal aneurysm.

Conclusions: The prevalence of all grades of PFO (22.6%) and open flap PFO (11.1% = grade 2 and 3) with this technique compares with 24.3% by trans-oesophageal echocardiography (TOE) and 14.9% by saline contrast echocardiography (SCE)[2, 3] Further comparative studies are required but we believe an open flap PFO or ASA should be identified and recorded during cardiac CT. This approach may identify those at risk of cryptogenic stroke as well as avoid unnecessary tests in stroke patients.

Keywords: Patent foramen ovale; atrial septum; cardiac anatomy; computed tomographic angiography; non-invasive angiography.

Although the primary clinical role of 64 Multi-detector coronary CT (64-MDCT) is assessment of the coronary arteries, the excellent spatial resolution of the technique allows detailed imaging of other cardiac structures during a routine "coronary" examination.[4] The inter-atrial septum (IAS) is one area that lends itself to such investigation, but it has been neglected in some otherwise comprehensive assessments of non-coronary cardiac CT pathology.[5, 6]

One study has however, looked at the prevalence of patent foramen ovale (PFO) in a mixed cohort of research volunteers and suspect ischaemic heart disease (IHD) patients using retrospective ECG gating –a relatively high dose technique by 2010 standards[7]. We set out to measure prospectively, the prevalence of PFO in a cohort of consecutive suspect IHD patients attending for routine coronary CT angiography using standard, everyday coronary protocols (including use of low-dose prospective ECG gated protocols as frequently as possible).

The IAS is formed from the union of two separate layers that form a flap valve in utero to facilitate the fetal circulation. Failure of the flap valve to close after birth can result in a PFO. This communication between right (RA) and left (LA) atria provides an anatomic substrate for paradoxical embolisation of thrombus and is strongly associated with cryptogenic stroke (CS).[8] An atrial septal aneurysm (ASA) can also occur and is associated with both PFO and CS.[8]

METHODS

The study was approved by the Western HSC Trust Research and Development (Ethics) Chair. Data was collected prospectively on patients attending for 64-MDCT between the 18th June 2009 and 27th February 2010.

COMPUTED TOMOGRAPHY

64-MDCT was performed using a Philips Brilliance 64 system (Philips Medical Systems, Eindhoven, Netherlands). Patients were monitored on electrocardiogram (ECG) and a 20FG intravenous cannula placed in an ante-cubital fossa vein. All patients were in sinus rhythm. After heart rate optimisation and sub-lingual administration of 400 micrograms of glyceryl tri-nitrate, non-ionic contrast material (Iohexol, Omnipaque

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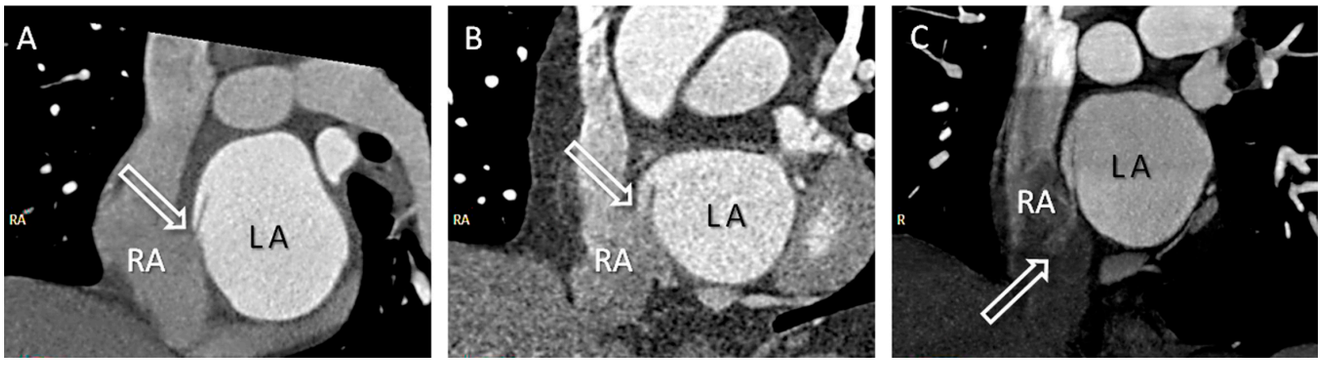

Fig 1. Panel A. Oblique coronal view: hollow arrow demonstrates closed flap (Grade 1 PFO), left atrium =LA, right atrium =RA. **Panel B.** Oblique coronal view: hollow arrow demonstrates open flap (Grade 2 PFO . **Panel C.** Oblique coronal view: hollow arrow demonstrates jet from open flap (Grade 3 PFO).

350, GE Healthcare AS, Norway) was injected into the vein (90 ml at a flow rate of 5.5 ml/sec followed by a saline chaser of 50mls at 5.5 ml/sec). A bolus tracking technique was used to determine when contrast density was optimal for coronary imaging. Scanning was performed during a single breath hold. In patients with a low and stable heart rate (<64 beats per minute), prospective ECG triggering was used for data acquisition; otherwise retrospective ECG gating was used. In all cases, data was obtained at a single time point (75% of the R-R wave interval on ECG). Detector collimation was 64 x 0.625mm with images reconstructed to a slice thickness of 0.6mm. Tube voltage was 120kV with a rotation time of 400 msec. Standard axial images and 2D multiplanar reformations were used for image interpretation. Coronal oblique projections through the IAS were specifically evaluated for the presence of each of the CT criteria for PFO outlined below.

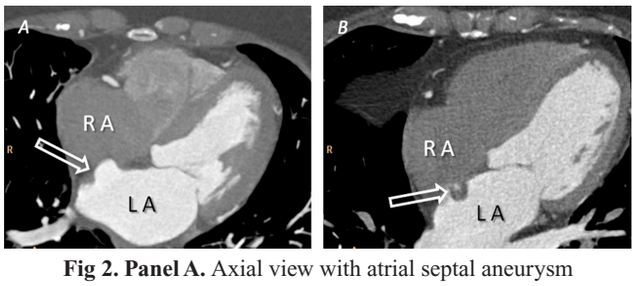

Fig 2. Panel A. Axial view with atrial septal aneurysm highlighted by hollow arrow, left atrium =LA, right atrium =RA. **Panel B.** A small rounded mass is identified over the fossa ovalis with a vascular supply (hollow arrow). This proved to be a left atrial myxoma.

CLASSIFICATION OF PFO AND ASA

Williamson *et al.* devised a classification system based in part on chart review of 20 patients with PFO who underwent both CT and Trans-oesophageal echocardiography (TOE).[1] PFO anatomy on 64-MDCT was classified by 3 criteria:

1. A distinct flap at the expected location in the LA (closed flap, Figure 1, panel A).
2. A continuous column of contrast material between the septum primum and septum secundum, connecting the LA and RA (open flap, Figure 1 panel B).
3. An open flap plus a jet of contrast material from the column into the RA (open flap with jet, Figure 1, panel C).

When compared with TOE diagnosis, the positive predictive value of criterion 1 alone was 75%, criteria 1 +2 together was 80% and 1+2+3 together was 100%.[1]

ASA was defined as a redundant and hyper-mobile portion of the IAS that demonstrated more than 10-mm excursion from the centre line (Figure 2, panel A).[9]

We also categorised any potential IAS source of cardio-embolism into medium and high risk according to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification.[10]

RESULTS

The study population consisted of 261 consecutive patients of whom 54% were male (mean age 56 years, range 21 to 81 years) and 46% were female (mean age 57 years, range 36 to 81 years). Study quality was sufficient for PFO classification in all cases. Study quality for coronary imaging was graded as excellent in 50%, good in 28%, fair in 16% and poor in 6%. A low dose prospective ECG triggered protocol was used in 38%. Results are displayed in Table 1. Amongst the 261 patients, 59 (22.6%) demonstrated a PFO. This could be subdivided into 30 (11.5%) with a grade 1 PFO, 17 (6.5%) with grade 2 and 12 (4.6%) with grade 3. In total, 29 (11.1%) of patients had an open channel between the atria during the CT scan (grade 2 or 3 PFO).

An atrial septal aneurysm was identified in 16 (6.1%) patients but no jet of contrast from left to right atrium was seen in association with this.

One patient was seen to have an early (1.1cm diameter) left atrial myxoma with prominent central vasculature (Figure 2, panel B).

Table 2 lists patients with conditions classified by the TOAST criteria for medium or high risk of cardiac embolism.[10] Of note, 17.2% of patients had medium cardio-embolic risk.

DISCUSSION

PFO is strongly linked with conditions such as CS, pulmonary embolus and more controversially, migraine with aura.[8, 11, 12] Major studies to determine the role of PFO closure devices are underway.[13] The reported prevalence of PFO depends

however, on the imaging modality used and the population studied. Prevalence based on normal heart autopsy is 27%, whilst SCE and TOE yield figures of 14.9% and 24.3% respectively in normal adults.[2, 3, 14]

Table 1.

Numbers and percentages of patients displaying conditions of the inter-atrial septum.

Condition	Number of Patients	Percentage of Total
Normal	185	70.9%
Myxoma	1	0.38%
Grade 1 PFO	30	11.5%
Grade 2 PFO	17	6.5%
Grade 3 PFO	12	4.6%
Atrial septal aneurysm	16	6.1%
All PFOs (Grades 1,2 +3)	59	22.6%
"Open" PFOs (Grades 2 +3)	29	11.1%

Table 1 Legend: PFO = patent foramen ovale. Graded by Williamson classification[1].

Prevalence is higher in vulnerable groups; amongst migraineurs in the MIST 1 study, a moderate or large PFO was detected in 37.7% by SCE, whilst 43.9% of young CS patients were demonstrated to have a PFO by TOE.[15, 16] TOE is regarded as the gold standard imaging technique for PFO assessment.[17, 18] Recently, real time 3D TOE has proved useful in guiding PFO closure device procedures.[19]

Moving away from echocardiography, only a handful of studies of PFO anatomy have been performed on 64-MDCT.[1, 7, 20, 21]

Table 2.

Conditions classified under the TOAST criteria for cardioembolic risk. (11)

Condition/Risk Status	Number of Patients	Percentage of Total
High-risk source		
Myxoma	1	0.38%
Medium-risk source		
Grade 2 or 3 PFO	29	11.1%
Atrial septal aneurysm	16	6.1%
TOTAL	**46**	**17.6%**

Table 2 Legend: PFO = patent foramen ovale. Graded by Williamson classification[1].

Two studies have concentrated on comparing 64-MDCT with TOE. Williamson *et al*. reviewed 214 charts of patients attending for 64-MDCT and found 20 who had also undergone TOE. Of the six with PFO on TOE, *all* had grade 1 or higher PFO by the criteria defined in that study.[1] Kim *et al.* retrospectively analysed images from 152 stroke patients who had undergone both TOE and CT. Twenty-six PFOs were identified by TOE with 19 of these patients having a grade 3 (open flap with jet) PFO appearance on CT.[20] The authors also noted a "channel-like appearance" of the IAS which corresponded to grade 1 (closed flap) and grade 2 (open flap) in the Williamson *et al.* paper. Compared with TOE, the two papers combined yield a sensitivity of 67-73%, specificity of 98-100%, positive predictive value of 91-100% and negative predictive value of 85-95% for a grade 3 CT appearance. In a more generalised study, CT was compared with TOE for detection of cardiac sources of embolism in 137 stroke patients.[21] Just under a quarter of the patients had PFO, ASA or an atrial septal defect identified by TOE. Overall sensitivity of CT was 89% with a positive predictive value of 100% for all embolic causes. The overall prevalence of all 3 grades of PFO in our study was 22.6%. We agree with previous authors that an open flap with direct communication between atria (grades 2 and 3) is more likely to represent clinically significant PFO, in which case, the prevalence falls to 11.1%.

STUDY LIMITATIONS

One major problem with assessing PFO by 64-MDCT is that the information is purely anatomical and obtained during a breath hold rather than Valsalva manoeuvre. The functional and flow information obtained with TOE cannot be emulated.

It is interesting to note that the prevalence of all 3 grades of PFO at 22.6% is very similar to TOE and autopsy reference data, perhaps some of the closed flaps (11.5%) would open if right atrial pressure was elevated. Unfortunately, the rise in central venous pressure associated with Valsalva manoeuvre or coughing also impedes the passage of intravenous contrast to the heart. Unacceptable respiratory motion artefacts would also be introduced.

Potentially, cine CT angiography[22] could give information about directional flow in a PFO and mobility of ASA, but the Valsalva manoeuvre problem would remain.

The point we wish to stress in this paper is that much useful information can be obtained during a routine coronary study without additional measures or high dose protocols.

The prevalence of ASA in our study (6.1%) falls within the range seen in TOE studies on non-stroke patients (4-8%) - this figure can rise up to 15 - 28% in stroke populations.[23, 24] We did not observe left to right contrast flow through an aneurysm but it is accepted that approximately 33% of adults with ASA also have PFO and ASA is considered a medium risk source of embolus by TOAST criteria.[8,9]

CURRENT GUIDELINES

The Society of Cardiovascular Computed Tomography (SCCT) guidelines on reporting studies state that any [non-coronary] abnormalities should be described and that cardiac chamber shunts are a required element of a comprehensive report[25] but given that 17.2% of our patients attending for routine coronary CT had a medium cardio-embolic risk (open flap PFO or ASA) perhaps more emphasis should be placed on this requirement.

CONCLUSIONS

64-MDCT allows accurate assessment of the IAS during routine "coronary" examination. We found the prevalence of open flap PFO and ASA to be 11.1% and 6.1% respectively

in a population of 261 patients undergoing routine 64-MDCT coronary study. Further comparative studies against SCE and TOE are required but we believe open flap PFO and ASA should be clearly identified and recorded during routine coronary CT angiography. This approach may identify those at risk of cryptogenic stroke as well as avoid unnecessary tests in stroke patients.

The authors have no conflict of interest.

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